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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/650,799	08/29/2003	Patricia B. Hoyer	241331US20	7462

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EXAMINER	
BERTOGLIO, VALARIE E	

ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
03/13/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/650,799	HOYER ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *02/23/2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *69-103* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *69-103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08/29/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/23/2009 has been entered.

Claims 69-70,83,86,91 are amended. Claims 95-103 are added. Claims 69-103 are pending and are under consideration in the instant office action.

Information Disclosure Statement

Applicant previously stated that a copy of the poster listed as reference AAJ at page 4 of the IDS dated 06/07/2007 was submitted with the reply dated 02/19/2008. The poster submitted 02/19/2008 is not a legible copy of the poster submitted 06/07/2007 but appears to be a different poster, (dated 2005 or later). The poster that should be considered for its relevance as art under 35 USC 102(a) and was listed on the IDS filed 06/07/2007 is titled "An ovary-intact mouse model that Mimics Perimenopause in Women".

The information disclosure statement filed 06/17/2008 fails to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement. The information

disclosure statement has been placed in the application file, but the information referred to therein has not been considered.

Claim Objections

Applicant is advised that should claim 86 be found allowable, claim91 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The scope of the claims appear to be the same. The effect of the ovarian failure on the population fails to add any additional limitation to the method steps as claimed.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 69-85 remain rejected and claims 86-103 are newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Claim 69 required a complete depletion of ovarian primordial follicles. Claim 83 is directed to a method of making the animal of claim 69. Claim 86 is drawn to a method of inducing ovarian failure, which requires full depletion of ovarian follicles as defines at page 12, lines 9-10 and 18-19.

The specification provides no implicit or explicit support for a complete depletion of primordial follicles using the conditions claimed. The specification teaches complete depletion of ovarian primordial follicles using 160mg/kg/day for a period of 15 days. The claims encompass total depletion using lower dosages for shorter time periods. The specification has only provided support for partial depletion of ovarian follicles expression of the DNA construct in the context of the claimed transgenic mouse. Page 12, lines 13-14 mentions a complete absence of primordial follicles, however, the specification does not associate this effect as having been obtained in the claimed animals. Treatments to obtain complete depletion of primordial follicles required greater amounts of VCD than that claimed (see pages 17-18 and Figures 1-2). Applicants are reminded that it is their burden to show where the specification supports any amendments to the claims. See 37 CFR 1.121 (b)(2)(iii), the MPEP 714.02, 3rd paragraph, last sentence and also the MPEP 2163.07, last sentence.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure* [or point to case law supporting incorporation of such a limitation as in the instant case]" (emphasis added).

Scope of enablement

Claims 69-103 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed methods in mice comprising administering at least 160 mg/kg/day for 15 days to cause complete depletion of ovarian follicles , ovarian failure or menopause, does not reasonably provide enablement for use of less than 160 mg/kg/day VCD for less than 15 days to cause complete depletion of ovarian follicles, ovarian failure or menopause or for causing complete ovarian follicle depletion in any species other than mouse as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

As set forth above, the claims encompass a broad range of administration protocols with a broad range of effects including complete depletion of ovarian follicles. Claim 69 recites complete depletion of ovarian follicles. Claim 86 recites ovarian failure. Claim 91 recites "at least" partial ovarian failure. The specification at page 12 states that "menopause" is defined as "complete ovarian failure" and for menopause, all ovarian follicles are depleted. Thus, the claims each encompass complete depletion of ovarian follicles. At page 21 the specification teaches the "optimal concentration of VCD (lowest amount, shortest time) was determined to be 160 mg/kg" injected once daily for 15 days. The claims encompass less VCD for a shorter time, including one day, to accomplish complete ovarian depletion.

The specification as well as the art at the time of filing shows that less than 160 mg/kg/day for 15 days does not cause complete ovarian depletion. Springer (1996, IDS) taught that 10 days of dosing reveals initial evidence of impending destruction of small preantral follicles although measurable reduction in oocyte numbers had not yet occurred. Hoyer et al (1991) taught that dosing rats for 30 days destroyed the majority of follicles. The art also teaches differences in susceptibility to VCD among different mammalian species with mice being more susceptible than rats (Hoyer, 1991, page 91; IDS). Examples 4 and 5 of the specification prophetically outline methods to be carried out to determine if shorter dosing regimens will be effective and what effects they will have on animals. This exemplifies the fact that further experimentation is required to determine if the range of dosage claimed will result in the bradth of phenotypes claimed.

The claims require an extreme phenotype of complete ovarian follicle depletion and the art teaches that mice are more susceptible than rats to VCD (see above). The specification does not provide any guidance with respect to what dosage regimen would be required to reach complete follicle depletion in rats or any other species other than mouse. Determining such would require undue experimentation.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 83-94 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of Applicant's amendments to the claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Valarie Bertoglio/
Primary Examiner, Art Unit 1632